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09/993,003	11/06/2001	Richard Allen Rosenbloom	QUIG-1006US	5759

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EXAMINER	
STILLER, KARL J	
ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/993,003	Applicant(s) ROSENBLOOM, RICHARD ALLEN
	Examiner Karl Stiller	Art Unit 1617

-- Th MAILING DATE of this communication appears on the cover sh et with the correspond nc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-11 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-11 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, and 6-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In the instant application, the inclusion of "one or more compounds that regulate at least one of cell differentiation and cell proliferation" in Claim 1, "vitamin D3 analogs" in Claim 2, "vitamin D3 derivatives which regulate at least one of cell differentiation and cell proliferation" in Claim 3, and "structurally similar derivatives [of the recited antioxidants] which exhibit antioxidant activity" in Claim 4, is not enabled by the specification. Attention is directed to *General Electric Company v. Wabash Appliance Corporation et al* 37 USPQ 466 (US 1938), at 469, speaking to functional language at the point of novelty as herein employed: "the vice of a functional claim exists not only when a claims is "wholly" functional, if that is ever true, but when the inventor is painstaking when he recites what has already been seen, and then uses conveniently functional language at the exact point of novelty". Functional language at the point of novelty, as herein employed by Applicants, is further admonished in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC

1997) at 1406: stating this usage does "little more than outlin[e] goals appellants hope the recited invention achieves and the problems the invention will hopefully ameliorate". Applicants functional language at the point of novelty fails to meet the requirements set forth under 35 USC 112, first paragraph. Claims employing functional language at the point of novelty, such as Applicants', neither provide those elements required to practice the inventions, nor "inform the public during the life of the patent of the limits of the monopoly asserted" *General,Electric Company v. Wabash Appliance Corporation et* supra, at 468. Claims 6-10 ultimately depend from Claim 1, and do not correct the deficiencies detailed above.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "structurally similar" in Claim 4 is a relative term which renders the claim indefinite. The phrase "structurally similar" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear as to what structural deviations from the recited compounds would be acceptable and to what extent these substitutions may be made and still allow the compound to be considered "structurally similar".

The term "substantially" in Claim 6 is a relative term which renders the claim indefinite. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear as to what standard the resulting topical composition is to be measured against to determine if it is a "substantially topical composition".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 6, 7, and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kita (WO97/18817) and Sine et al. (US 5,972,359) in view of "Sports Medicine Articles".

Kita discloses a composition comprising the cell proliferation and differentiating compound, vitamin D3 (also known as cholecalciferol and calcitriol) in the non-USP hydrophilic ointment base, hydrophilic petrolatum (see column 10, PREPARATION 5, lines 45-54). Kita also discloses that the vitamin D3 composition is useful in a method to treating skin to protect against the effects of ultraviolet radiation (see column 9, lines 43-48, column 10, lines 50-54).

Sine et al. discloses a method of treating skin to reduce the effects of ultraviolet radiation exposure (sun exposure), comprising applying a composition that comprises the antioxidants, tocopherol (vitamin E) acetate and retinal (vitamin A), and D-panthenol, in a pharmaceutically acceptable carrier comprising the acrylic copolymers, Carbopol® 954 and Carbopol® 1382 (which are known copolymers of acrylic acid and a polyallyl sucrose) which are dissolved in PEG-100 stearate (polyethylene glycol) (see column 3, lines 30-35, column 39, especially Phase C, items 3 and 4, Phase D, items 4 and 9, Phase F, item 1, Phase H, item 3, lines 36-67).

The primary references do not particularly disclose methods comprising an effective amount of vitamin D3 and vitamin A and/or vitamin E acetate, with or without D-panthenol, and with or without Carbopol® 954 and Carbopol® 1382 dissolved in PEG-100 stearate.

"Sports Medicine Articles" discloses that actinic (radiation) dermatitis (inflammation of the skin) results from exposure of the skin to ultraviolet radiation from the sun (see p. 1, lines 1-10, p.1, line 33 through p. 2, line 1).

It would have been obvious at the time the invention was made to modify the primary references by employing a composition comprising an effective amount of vitamin D3 and vitamin A and/or vitamin E acetate, with or without D-panthenol, and with or without Carbopol® 954 and Carbopol® 1382 dissolved in PEG-100 stearate in a method of treating and/or preventing radiation dermatitis caused by sun exposure.

One of ordinary skill would have been motivated to employ a composition comprising an effective amount of vitamin D3 and vitamin A and/or vitamin E acetate,

with or without D-panthenol, and with or without Carbopol® 954 and Carbopol® 1382 dissolved in PEG-100 stearate in a method of preventing and/or treating radiation dermatitis caused by sun exposure since the primary references teach the desirability of employing the same actives and excipients in compositions and methods to prevent and/or treat ultraviolet radiation induced effects on sun exposed skin, for example, radiation dermatitis. Their combination into a single method to prevent or treat radiation dermatitis is considered prima facie obvious. Prophylactic as well as treatment activity of the combination against radiation dermatitis would be reasonably expected based on the prior art (see, for example, Kita, column 9, lines 43-48, column 10, lines 45-54, Sine et al., column 3, lines 30-35, column 39, especially Phase C, items 3 and 4, Phase D, items 4 and 9, Phase F, item 1, Phase H, item 3, lines 36-67). It is prima facie obvious to combine in a method of preventing and/or treating the ultraviolet radiation induced effects on sun exposed skin, such as radiation dermatitis, vitamin D3 (with or without a non-USP hydrophilic ointment base), at least one antioxidant, such as vitamin A or vitamin E acetate (with or without D-panthenol, and with or without Carbopol® 954 and Carbopol® 1382 dissolved in PEG-100 stearate), in order to form a single method that is to be used for the very same anti-radiation dermatitis purpose; the idea of combining them flows logically from their having been individually taught in the prior art. See *In re Kerkhoven*, 205 USPQ 1069, CCPA 1980.

Additionally, one of ordinary skill would have been motivated to employ the effective amount of vitamin D3 and vitamin A and/or vitamin E acetate herein since the optimization of dosage ranges for a drug regimen for active agents is considered within

the skill of the artisan as optimization of a result effective parameter. See *In re Boesch* 205 USPQ 215.

Claims 5, 8, 10, and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kita (WO97/18817-US 6,162,801 is used herein as an English translation) and Sine et al. (US 5,972,359) in view of "Sports Medicine Articles" (above), and further in view of Neigut (US 6,048,886), Schonrock et al. (US 5,876,737), and Gers-Barlag et al. (US 5,952,391).

Kita and Sine et al., and "Sports Medicine Articles" (above) suggests a composition comprising the cell proliferation and differentiation regulating compound, vitamin D3, the antioxidants, vitamin A and vitamin E acetate, and a method of treating and/or preventing radiation dermatitis caused by sun exposure, comprising the topical application of the same (see above).

Kita and Sine et al., and "Sports Medicine Articles" do not expressly disclose the employment of α-lipoic acid, or hydroxymethylcellulose, or one or more antioxidant enzymes, in the method for treating radiation dermatitis suggested therein. Kita and Sine et al., and "Sports Medicine Articles" also do not expressly disclose a composition comprising the actives and excipients herein in the particular amount ranges recited herein (see Claim 11).

Neigut discloses a composition comprising vitamin A, vitamin D, vitamin E, ascorbyl palmitate, α-lipoic acid, and the antioxidant enzyme, superoxide dismutase, in a corn oil vehicle, and a method of preventing and/or treating sun induced ultraviolet radiation damage, such as dermatitis, comprising the topical application of the same

(see column 1, lines 42-46, column 4, lines 38-60, column 5, lines 29-35, column 7, Compound II, lines 40-60, column 11, line 59 through column 13, line 60).

Schonrock et al. discloses a sunscreen composition comprising α-tocopherol acetate (vitamin E acetate), and hydroxypropylmethylcellulose that is useful in a method of preventing and/or treating sun induced ultraviolet radiation damage, such as inflammation, comprising the topical application of the same (see column 1, line 66 through column 2, line 5, lines 39-44, column 14, lines 1-44). Schonrock et al. also suggests the interchangeability of hydroxypropylmethylcellulose and hydroxymethylcellulose in the disclosed compositions (see column 12, lines 4-7).

Gers-Barlag et al. discloses a sunscreen composition comprising quercetin that is useful in a method of preventing and/or treating sun induced ultraviolet radiation damage, comprising the topical application of the same (see column 1, line 6 through column 2, line 28, column 14, line 25 through column 15, line 20).

The references do not particularly disclose a method of treating and/or preventing radiation dermatitis caused by sun exposure, comprising the employment of a composition comprising vitamin D3, vitamin A, vitamin E acetate, and α-lipoic acid. The references also do not particularly disclose the same method, comprising the employment of vitamin D3, at least one antioxidant, such as vitamin A or vitamin E, further employing hydroxymethylcellulose as the pharmaceutically acceptable carrier, or further employing one or more antioxidant enzymes, such as superoxide dismutase. The references also do not particularly disclose a topical composition comprising vitamin A, vitamin D3, vitamin E acetate, ascorbyl palmitate, quercetin, α-lipoic acid, and

a pharmaceutically acceptable carrier, or the particular amounts of each recited herein (see Claim 11).

It would have been obvious at the time the invention was made to modify the references by combining the method suggested by Kita, Sine et al., and "Sports Medicine Articles" (see above) of treating radiation dermatitis employing vitamin D3, vitamin E acetate, and vitamin A by also employing α-lipoic acid and/or hydroxymethylcellulose as a carrier, and/or one or more antioxidant enzymes, such as superoxide dismutase, and/or quercetin, and/or a corn oil base carrier in the amounts recited herein in a topical composition for the same purpose.

One of ordinary skill would have been motivated to employ a composition comprising an effective amount of a cell proliferation and differentiation regulator, such as vitamin D3, and an effective amount of at least one antioxidant, such as vitamin A and/or vitamin E acetate and/or one or more antioxidant enzymes, such as superoxide dismutase, with or without α-lipoic acid, with a pharmaceutically acceptable carrier, in a method of treating and/or preventing radiation dermatitis caused by sun exposure since the references teach the desirability and usefulness of the same actives and excipients in compositions and methods to prevent and/or treat ultraviolet radiation induced effects on sun exposed skin, for example, radiation dermatitis. The combination of the anti-radiation actives herein into a single method to prevent or treat radiation dermatitis is considered prima facie obvious. Prophylactic as well as treatment activity of the combination against radiation dermatitis would be reasonably expected based on the prior art (see, for example, Kita, column 9, lines 43-48, column 10, lines 45-54, Sine et

al., column 3, lines 30-35, column 39, especially Phase C, items 3 and 4, Phase D, items 4 and 9, Phase F, item 1, Phase H, item 3, lines 36-67, Neigut, column 1, lines 42-46, column 4, lines 38-60, column 5, lines 29-35, column 7, Compound II, lines 40-60, column 11, line 59 through column 13, line 60, Schonrock et al., column 1, line 66 through column 2, line 5, lines 39-44, column 12, lines 4-7, column 14, lines 1-44, and Gers-Barlag et al., column 1, line 6 through column 2, line 28, column 14, line 25 through column 15, line 20). It is prima facie obvious to combine a cell proliferation and differentiation regulator, such as vitamin D3, at least one antioxidant, such as vitamin A, and/or vitamin E acetate, and/or one or more antioxidant enzymes, such as superoxide dismutase, with or without α-lipoic acid, in order to form a single method or composition that is to be used for the very same anti-radiation dermatitis purpose; the idea of combining them flows logically from their having been individually taught in the prior art. See *In re Kerkhoven*, 205 USPQ 1069, CCPA 1980.

Further, one of ordinary skill would have been motivated to employ hydroxymethylcellulose as a carrier in the anti-radiation composition herein since Schonrock et al. discloses an anti-radiation composition comprising hydroxypropylmethylcellulose as a carrier and suggests the interchangeability of hydroxypropylmethylcellulose and hydroxymethylcellulose in the same composition (see column 12, lines 4-7).

One of ordinary skill would also have been motivated to employ vitamin D3 and vitamin A in a corn oil base, vitamin E acetate, ascorbyl palmitate, quercetin, and α-lipoic acid in a single topical composition in a pharmaceutically acceptable carrier, as in

Claim 11, since the references teach the desirability of employing the same actives and excipients in compositions and methods to prevent and/or treat ultraviolet radiation induced effects on sun exposed skin, for example, radiation dermatitis. Their combination into a single composition useful for the same purpose is considered prima facie obvious. The idea of combining them flows logically from their having been individually taught in the prior art. See *In re Kerkhoven*, 205 USPQ 1069, CCPA 1980.

Additionally, one of ordinary skill would have been motivated to employ the amounts of actives and excipients recited herein since the optimization of dosage ranges for a drug regimen is considered within the skill of the artisan as optimization of a result effective parameter. See *In re Boesch* 205 USPQ 215. Applicant has not demonstrated the criticality of the amounts of actives and excipients recited herein.

Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karl Stiller whose telephone number is 703-306-3219. The examiner can normally be reached Monday through Friday, 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie can be reached at 703-308-4612. The fax phone number for the organization where this application or proceeding is assigned is 703-308-4556 for regular communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Stiller: ks
January 14, 2002

MINNA MOEZIE, J.D.
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